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January 3, 2005
Date

Monica A. De La Paz

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Philip D. Ashton-Rickardt
Joseph T. Opferman

Serial No.: 09/993,363

Filed: November 14, 2001

For: INDUCTION OF IMMUNITY USING INHIBITORS OF GRANZYMES

Group Art Unit: 1632

Examiner: Ram R. Shukla

Atty. Dkt. No.: ARCD:382US

REPLY BRIEF

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REPLY BRIEF

M.S. APPEAL BRIEF - PATENTS
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Appellants hereby submit an original and two copies of this Reply Brief in response to the Examiner's Answer dated November 2, 2004. The deadline for this reply is January 2, 2005. No fees are believed due; however, should any fees be due, the Commissioner is authorized to withdraw the appropriate fee from Fulbright & Jaworski Deposit Account No. 50-1212/ARCD:382US. Please date stamp and return the enclosed postcard to evidence receipt of this document.

Also enclosed herewith is a request for oral argument, and fees therefor. If the request and fees are missing, please consider this to be such a request, and authorization to debit the aforementioned deposit account number.

I. SUMMARY OF ISSUES AND APPELLANT'S REPLY

A. Claims 26-35, 37, 42-44, 48-50, 61-65, 67, and 71-73 as rejected as not meeting the written description requirement of 35 U.S.C. §112, first paragraph, because the Specification allegedly fails to describe a representative number of species of serpin or serpin mimetics encompassed by the claimed invention and their identifying characteristics.

This rejection is overcome by the evidence of record. For example, Appellants have cited in their response a substantial amount of information from the Specification pertaining to members of the genus of serpins and serpin mimetics, including specific and identifying characteristics of the serpins and serpin mimetics of the claimed invention. The information cited by Appellants in the Specification meets the written description requirement because it "clearly allows person of ordinary skill in the art to recognize that [the inventors] invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

B. Claims 26-35, 37-40, 42-44, 48-50, and 61-74 are rejected as not meeting the enablement requirement of 35 U.S.C. §112, first paragraph, because the art of gene therapy or therapy of a viral infection with CTLs is said to be unpredictable, and the Specification does not provide guidance as to how to address the issue of unpredictability. Further, it is said that the Specification does not teach how to induce immunity in an HIV infected subject or any subject with any viral infection by the claimed methods.

This rejection is overcome by the evidence of record. The enablement requirement of 35 U.S.C. §112, first paragraph, has been met because Appellants have demonstrated by argument and evidence, including the declaration of Raymond Welsh, Ph.D. (previously submitted as part of the response to the Office Action dated June 17, 2003 and the Appeal Brief dated April 22,

2004), that "any person skilled in the art can make and use the invention without undue experimentation." *In re Wands*, 858 F.2d.731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

II. REPLY

A. There is Adequate Written Description Support for Claims 26-35, 37, 42-44, 48-50, 61-65, 67, and 71-73 in the Specification

According to the Examiner's Answer, claims 26-35, 37, 42-44, 48-50, 61-65, 67, and 71-73 stand rejected as not meeting the written description requirement of 35 U.S.C. §112, first paragraph, because the Specification allegedly fails to describe a representative number of species of serpin or serpin mimetics encompassed by the claimed invention and their identifying characteristics. See Examiner's Answer, page 3, paragraph 3 through page 5, paragraph 2. Appellants note as an initial matter that a description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the Examiner to rebut the presumption. *Manual of Patenting Examining Procedure*, §2163.04, citing *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The Examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description. *MPEP* §2163.04. No such basis has been set forth by the Examiner in any of the Office Actions or the Examiner's Answer.

According to the Examiner's Answer, in order to meet the written description requirement of 35 U.S.C. §112, first paragraph, Appellants must provide detailed exemplary information, including detailed structural information, pertaining to members of each and every subgenus of the genus of serpins and serpin mimetics. See Examiner's Answer, page 4, paragraph 1 through page 5, paragraph 2. However, this is not the standard for compliance with the written description requirement set forth by the law. To meet with written description requirement, the description must convey with reasonably clarity to those skilled in the art that,

as of the filing date sought, an Applicant was in possession of the invention, and the invention, in that context, is whatever is now claimed. See *Vas-Cath, Inc., v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991).

As previously set forth in the Appeal Brief, Appellants have demonstrated that the instant Specification discloses a substantial amount of information pertaining to the genus of serpins and serpin mimetics. Representative members of the genus of serpins and serpin mimetics have been cited, including particular serpins useful in the context of the invention, and detailed information pertaining to structural and functional characteristics of members of this genus. See, *e.g.*, Specification, page 4, lines 20-26; page 5, lines 21-23; page 6, lines 21-24; page 15, lines 15-16; Page 15, line 21 through page 16, line 4; Page 19, lines 12-14; Page 37, lines 22-24. In addition, each of the Examples delineated in the Specification provides substantial information pertaining to serpins, in particular SPI6 and PI9, in the context of the present invention. Specification, Examples 1-13 (page 67, line 22 through page 89, line 4).

The substantial information in the instant Specification pertaining to serpins and serpin mimetics, including information that is functional as to any conceivable subgenuses, is sufficient to meet this threshold requirement for written description. One of ordinary skill in the art, based on the disclosure set forth pertaining to serpins and serpin mimetics in the Specification, would understand that Appellants were in possession of the invention set forth in the claims – that is the burden that has been met by Appellants, and that is all that is required of Appellants.

Accordingly, because the information set forth in the Specification is sufficient to reasonably convey to one skilled in the art that Appellants were in possession of the genus of serpins and serpin mimetics at the time the invention was filed, the written description requirement has been met.

B. The Evidence and Argumentation Set Forth by Appellants is Sufficient to Meet with Enablement Requirement of 35 U.S.C. §112, First Paragraph

Claims 26-35, 37-40, 42-44, 48-50, and 61-74 stand rejected as not meeting the enablement requirement of 35 U.S.C. §112, first paragraph, because the Examiner's Answer alleges that the Specification as filed does not provide sufficient guidance for an artisan of skill to make and use the claimed invention, and an artisan of skill would have required undue experimentation to practice the claimed invention because the art of gene therapy or therapy of a viral infection with CTLs is unpredictable. See Examiner's Answer, page 5, paragraph 3. Further, the Examiner's Answer indicates that the Specification does not teach how to induce immunity in an HIV infected subject or any subject with any viral infection by the claimed methods. See Examiner's Answer, page 6, paragraph 1.

Regarding the issue of unpredictability of gene therapy and cell therapy, Appellants have previously noted that even though gene therapy and cell therapy using CTLs may not be commonplace today from a clinical standpoint, they most certainly are sufficiently enabling for patenting. Controlling precedent makes it clear that even those therapies ultimately without use in the clinic are of value, and therefore may be patented. *In re Krimmel*, 130 U.S.P.Q. 215, 219 (C.C.P.A. 1961). While each case is taken on its own merits, the PTO cannot cling to the notion that gene therapy or CTL therapy is *per se* lacking in enablement. It is critical to make the distinction between the necessary showing under 35 U.S.C. §112, first paragraph, and that needed to establish clinical efficacy.

The test of enablement under 35 U.S.C. §112, first paragraph, is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. See *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988); *United States v. Telectronics, Inc.*, 857 F.2d 778,

785, 8 U.S.P.Q.2d 1217, 1223 (Fed. Cir. 1988). Appellants have demonstrated by argument and evidence, including the declaration of Raymond Welsh, Ph.D., that "any person skilled in the art can make and use the invention without undue experimentation." *In re Wands*, 858 F.2d.731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Regarding the Declaration of Dr. Welsh, the Examiner argues that the Declaration establishes that LCMV infection has some resemblance to HIV infection, but does not establish that LCMV infection is an art-recognized model of HIV infection. However, Dr. Welsh, a skilled virologist who understands the immunology of viral infections, has declared that "[a] skilled virologist with an ordinary understanding of viral immunology would have recognized, at the time the above-referenced application was filed, that LCMV infection in mice is a model for determining the usefulness of the claimed invention for treating other viral diseases, including HIV." Appendix C, page 3, paragraph 7. He also declares that "a skilled virologist with an ordinary understanding of viral immunology would have understood, at the time the above-referenced application was filed, that LCMV infection in mice was a model for HIV infection in humans." Appendix C, page 3, paragraph 7. Dr. Welsh notes that his position with respect to the accepted nature of the LCMV mouse model is supported by literature, cited in detail in the Appeal Brief, that would be familiar to one having an ordinary understanding of viral immunology. Appendix C, page 3, paragraph 8. Thus, the Declaration of Dr. Welsh establishes that LCMV infection is an art-recognized model of HIV infection.

The Examiner's Answer argues that the Specification does not provide any specific information pertaining to how the methods of enhancing or inducing immunity to any viral infection, in particular HIV, will be practiced by providing an expression vector encoding a serpin or serpin mimetic. See Examiner's Answer, page 9, paragraphs 1-2 and page 14,

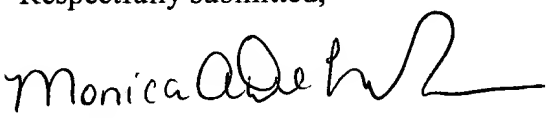
paragraph 1. The Examiner's Answer also argues that the LCMV mouse, as a transgenic mouse, is not a model for gene therapy, and does not address the issue of CTL transplantation. See Examiner's Answer, page 14, paragraph 2 through page 15, paragraph 1. Appellants, however, have established in the Appeal Brief that the Specification provides a substantial amount of information pertaining to serpins, serpin mimetics, and the treatment of viral disease, including enhancing or inducing immunity to a viral infection. This information in the Specification is sufficient to enable one of ordinary skill in the art to be able to make and/or use the claimed invention without undue experimentation. Enablement of the claimed invention is further evidenced by the Declaration of Dr. Welsh, who declares that based on his review of the cited references and sections of the Specification, "the present claims contain subject matter which was described in the Specification in such a way as to enable a skilled virologist with an ordinary understanding of viral immunology to make and/or use the invention." Further, Dr. Welsh has declared that "no undue experimentation would be required for a skilled virologist with an ordinary understanding of viral immunology to make and/or use the claimed invention of the above-referenced application as it is currently claimed." Appendix C, page 8, paragraph 12.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. See *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988); *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 U.S.P.Q.2d 1217, 1223 (Fed. Cir. 1988). Appellants have established, through argumentation with citations to the Specification along with the declaratory evidence of Dr. Welsh, that one of ordinary skill in the art would be able to make and/or use the claimed invention without undue experimentation. Therefore, the enablement rejection under 35 U.S.C. §112, first paragraph, should be overturned by the Board.

III. CONCLUSION

In light of the foregoing, Appellants submit that the claims on appeal should not be rejected under 35 U.S.C. §112, first paragraph, on the basis of written description and enablement. Therefore, the Board is requested to overturn the rejections.

Respectfully submitted,



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Date: January 3, 2005

APPENDIX 1: PENDING CLAIMS

26. A method for enhancing or inducing immunity to a viral infection comprising expressing a serpin or a serpin mimetic in a cytotoxic T-lymphocyte of a subject by introducing an expression construct comprising a DNA segment encoding the serpin or serpin mimetic under the control of a promoter active in the cytotoxic T-lymphocyte.

27. The method of claim 26, wherein enhancing or inducing immunity comprises increasing the number of cytotoxic T-lymphocyte memory cells.

28. The method of claim 26, wherein enhancing or inducing immunity comprises augmenting cytotoxic T-lymphocyte function.

29. The method of claim 26, wherein enhancing or inducing immunity comprises augmenting cytotoxic T-lymphocyte memory cell development.

30. A method for enhancing or inducing immunity to a virus comprising:

a) obtaining a cytotoxic T-lymphocyte that comprises an expression vector that comprises a DNA segment encoding a serpin or a serpin mimetic under the control of a promoter active in the cytotoxic T-lymphocyte; and

b) administering the cytotoxic T-lymphocyte to a subject in need thereof.

31. The method of claim 30, wherein the expression vector is a viral expression construct.

32. The method of claim 31, wherein the viral expression construct is selected from the group consisting of a retrovirus, an adenovirus, an adeno-associated virus, a herpesvirus, a polyoma virus, and a vaccinia virus.

33. The method of claim 31, wherein the vector is a retroviral vector.

34. The method of claim 30, wherein the serpin or serpin mimetic inhibits granzyme activity, inhibits granzyme transcription, inhibits granzyme translation, increases granzyme degradation, or destabilizes granzyme.

35. The method of claim 30, wherein the serpin or serpin mimetic inhibits granzyme function.

37. The method of claim 30, wherein the serpin or serpin mimetic is a serpin.

38. The method of claim 30, wherein the serpin is SPI6, PI9, PI-6, monocyte neutrophil elastase inhibitor (MNEI), PI-8, plasminogen activator inhibitor 2 (PAI-2).

39. The method of claim 38, wherein the serpin is SPI6.

40. The method of claim 38, wherein the serpin is PI9.

42. The method of claim 30, wherein the virus is HIV, LCMV, HCV, HTLV-1, HTLV-2, EBV, HBV, human cytomegatovirus, Herpes simplex 1, Herpes simplex 2, hepatitis G, enterovirus, dengue fever virus, or rabies virus.

43. The method of claim 42, wherein the virus is HIV.

44. The method of claim 42, wherein the virus is LCMV.

48. The method of claim 30, wherein inducing or enhancing immunity comprises increasing the number of cytotoxic T-lymphocyte memory cells.

49. The method of claim 30, wherein inducing or enhancing immunity comprises augmenting cytotoxic T-lymphocyte function.

50. The method of claim 30, wherein inducing or enhancing immunity comprises augmenting cytotoxic T-lymphocyte memory cell development.

61. The method of claim 26, wherein the expression construct is a viral expression construct.

62. The method of claim 61, wherein the viral expression construct is selected from the group consisting of a retrovirus, an adenovirus, an adeno-associated virus, a herpesvirus, a polyoma virus, and a vaccinia virus.

63. The method of claim 62, wherein the expression construct comprises a retroviral vector.

64. The method of claim 26, wherein the serpin or serpin mimetic inhibits granzyme activity, inhibits granzyme transcription, inhibits granzyme translation, increases granzyme degradation, or destabilizes granzyme.

65. The method of claim 26, wherein the serpin or serpin mimetic inhibits granzyme function.

66. The method of claim 26, wherein the serpin or serpin mimetic is PI9 or a PI9 mimetic.

67. The method of claim 26, wherein the serpin or serpin mimetic is a serpin.

68. The method of claim 67, wherein the serpin is SPI6, PI9, PI-6, monocyte neutrophil elastase inhibitor (MNEI), PI-8, plasminogen activator inhibitor 2 (PAI-2).

69. The method of claim 68, wherein the serpin is SPI6.

70. The method of claim 68, wherein the serpin is PI9.

71. The method of claim 26, wherein the virus is HIV, LCMV, HCV, HTLV-1, HTLV-2, EBV, HBV, human cytomegatovirus, Herpes simplex 1, Herpes simplex 2, hepatitis G, enterovirus, dengue fever virus, or rabies virus.

72. The method of claim 69, wherein the virus is HIV.

73. The method of claim 69, wherein the virus is LCMV.

74. The method of claim 30, wherein the serpin or serpin mimetic is PI9 or a PI9 mimetic.

APPENDIX 2

EXHIBIT A – SUMMARY OF CASES AND STATUTES

CASES

In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).
In re Wands, 858 F.2d.731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Vas-Cath, Inc., v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991).

United States v. Telectronics, Inc., 857 F.2d 778, 785, 8 U.S.P.Q.2d 1217, 1223 (Fed. Cir. 1988).

In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971).

STATUTES

35 U.S.C. §112, first paragrap

OTHER
Manual of Patent Examining Procedure, §2163.04.